

Applicant: Boldogh et al.

Serial No.: 10/691,330

Filed: October 22, 2003

Title: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF AS INHIBITORS OF APOPTOSIS AND OTHER CELLULAR DAMAGE

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

Listing of Claims

1. (Currently amended) A method for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof;

wherein the constituent peptide of colostrinin is selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO: 8);

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO:8); and further wherein the active analog inhibits apoptosis in a cell;

and wherein the apoptosis inhibitor inhibits apoptosis in the cell.

2. (Original) The method of claim 1 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

3. (Original) The method of claim 1 wherein the cell is a mammalian cell.

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4. (Original) The method of claim 3 wherein the cell is a human cell.
5. (Currently amended) The method of claim 1 wherein the inhibitor is ~~a constituent peptide of colostrinin~~.
6. (Currently amended) The method of claim [[5]] 1 wherein the inhibitor is a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), ~~VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPPFKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEELKSL (SEQ ID NO:30), VESYVPLFP (SEQ ID NO:31), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34)~~; and combinations thereof.
7. (Currently amended) A method for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof, ~~wherein;~~
wherein the constituent peptide of colostrinin is selected from the group consisting of MQPPPLP (SEQ ID NO:1) LQTPQPLLQVMMEPQGD (SEQ ID NO:2),

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DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLVLP (SEQ ID NO:4),

DLEMPVLVPEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6),

VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO: 8);

~~the active analog is an active analog of a constituent peptide of colostrinin selected from the group of SEQ ID NO:1 through SEQ ID NO:34;~~

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more constituent peptides of colostrinin; a constituent peptide of colostrinin selected from the group consisting of MOPPPLP (SEQ ID NO:1) LQTPQPLLOVMMEPOGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLVLP (SEQ ID NO:4), DLEMPVLVPEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO:8); and further wherein the active analog does not interfere with cellular uptake of redox-sensitive 2',7'-dihydro-dichlorofluorescein-diacetate;

and wherein the apoptosis inhibitor inhibits apoptosis in the cell.

8. (Original) The method of claim 7 wherein the apoptosis is due to DNA damage.
9. (Original) The method of claim 7 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.
10. (Original) The method of claim 7 wherein the cell is a mammalian cell.
11. (Original) The method of claim 10 wherein the cell is a human cell.
12. (Currently amended) A method for protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group

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consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof;

wherein the constituent peptide of colostrinin is selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO: 8);

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO:8); and further wherein the active analog does not interfere with cellular uptake of redox-sensitive 2',7'-dihydro-dichlorofluorescein-diacetate;

and wherein the compound protects the cell against DNA damage.

13. (Original) The method of claim 12 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.
14. (Original) The method of claim 12 wherein the cell is a mammalian cell.
15. (Original) The method of claim 14 wherein the cell is a human cell.

Amendment and Response

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16. (Withdrawn) A method for reducing the toxic effect of β -amyloid on a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof.

17. (Withdrawn) The method of claim 16 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

18. (Withdrawn) The method of claim 16 wherein the cell is a mammalian cell.

19. (Withdrawn) The method of claim 18 wherein the cell is a human cell.

20. (Withdrawn) A method for reducing the toxic effect of retinoic acid on a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof.

21. (Withdrawn) The method of claim 20 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

22. (Withdrawn) The method of claim 20 wherein the cell is a mammalian cell.

23. (Withdrawn) The method of claim 22 wherein the cell is a human cell.

24. (Cancel)